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For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: PREVENTION, THERAPY AND PROGNOSIS/MONITORING IN SEPSIS AND SEPTIC SHOCK

(57) Abstract: The invention relates to the use of a peptide which binds to lipopolysaccharide (LPS) or lipoteichoic acid (LTA), for manufacturing a pharmaceutical composition for treating sepsis or septic shock, wherein the peptide comprises the amino acid sequence of apolipoprotein CI (apoCI) or a part thereof that comprises at least the amino acids of the C-terminal helix of apoCI. The use of human apoCI is preferred. The peptide can be administered clinically to patients who have sepsis or threaten to develop sepsis. Measurement of the apoCI content in blood can be utilized for determining the severity and prognosis of the course of the septic condition or for monitoring an anti-sepsis treatment.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/NL 03/00475

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K38/17 A61M1/36 G01N33/68 A61P31/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K A61M C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, PAJ, WPI Data, MEDLINE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 747 455 A (NOVITSKY THOMAS J ET AL) 5 May 1998 (1998-05-05) column 2, line 55 -column 3, line 20; claims; figures 15,16; examples	1-11
A	J.W. LARRICK ET AL.: "A novel granulocyte-derived peptide with lipopolysaccharide-neutralizing activity." JOURNAL OF IMMUNOLOGY, vol. 152, 1994, pages 231-240, XP002236820 BALTIMORE, US cited in the application page 236, right-hand column, line 5 -page 238, right-hand column, last line; figure 1; table III	1-11

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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
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- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

14 October 2003

Date of mailing of the international search report

23/10/2003

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INTERNATIONAL SEARCH REPORT

Intern. Application No.

PCT/NL 03/00475

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 99 17740 A (DASSEUX JEAN LOUIS) 15 April 1999 (1999-04-15) page 6, line 23 - line 37; claims 1-5, 10-15, 31-34 page 7, line 34 - page 8, line 2 page 18, line 1 - line 13 -----	1-11
A	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; February 2001 (2001-02) BARLAGE STEFAN ET AL: "ApoE-containing high density lipoproteins and phospholipid transfer protein activity increase in patients with a systemic inflammatory response." Database accession no. PREV200100192387 XP002236821 abstract & JOURNAL OF LIPID RESEARCH, vol. 42, no. 2, February 2001 (2001-02), pages 281-290, ISSN: 0022-2275 cited in the application -----	1-11

INTERNATIONAL SEARCH REPORT

Inte application No.
PCT/NL 03/00475

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 8 and 9 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No.

PCT/NL 03/00475

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5747455	A	05-05-1998	US 5594113 A	14-01-1997
			US 6222021 B1	24-04-2001
			US 5627266 A	06-05-1997
			US 5614369 A	25-03-1997
			US 6384200 B1	07-05-2002
			AU 2006892 A	30-12-1992
			DE 69232307 D1	31-01-2002
			DE 69232307 T2	18-07-2002
			EP 0586573 A1	16-03-1994
			WO 9220715 A1	26-11-1992
			AT 207205 T	15-11-2001
			AU 3772289 A	12-01-1990
			CA 1338836 C	07-01-1997
			DE 68925275 D1	08-02-1996
			DE 68925275 T2	22-08-1996
			DE 68929334 D1	22-11-2001
			EP 0379549 A1	01-08-1990
			EP 0687911 A2	20-12-1995
			JP 2774343 B2	09-07-1998
			JP 3501733 T	18-04-1991
			WO 8912644 A1	28-12-1989
WO 9917740	A	15-04-1999	US 6287590 B1	11-09-2001
			AU 749344 B2	27-06-2002
			AU 9671598 A	27-04-1999
			CA 2305704 A1	15-04-1999
			CN 1280490 T	17-01-2001
			EP 1019025 A1	19-07-2000
			HU 0003930 A2	28-05-2001
			JP 2001522781 T	20-11-2001
			NO 20001683 A	10-05-2000
			NZ 503721 A	31-08-2001
			PL 339654 A1	02-01-2001
			WO 9917740 A1	15-04-1999
			US 6455088 B1	24-09-2002